

**242 The impact of a referral pathway on management of CFRD**M. Rezaie, K. Bailey, J. Lee, L. Speight, R.I. Ketchell. *I. Adult CF Centre, Cardiff, United Kingdom.*

There has been an increase in diagnosis of CFRD & IGT which may lead to a decline in pulmonary function (PF). This has been shown in our centre following the introduction of Annual Review (AR) since June 2005.

**Aim:** To develop a referral pathway for the management of CFRD.

**Methods:** A multidisciplinary approach was used involving CF and Diabetic Team (DT). The WHO protocol for OGTT formed the basis of the pathway. Three categories were defined: normal, IGT&CFRD. The IGT were classified into 2 groups; clinically stable & deteriorating (decrease weight and PF). Clinically stable patients monitored pre & post prandial for 2 weeks. Those with normal Blood Glucose Levels (BGL) had a repeat OGTT in a year. Those with normal pre, but raised post BGL were referred to the CF dietitian (CFD); those with raised pre & post BGL were referred to the DT&CFD. Deteriorating & CFRD patients were referred to the DT, CFD & were quarterly reviewed in a joint CF/DM clinic.

**Results:** see tables 1&2.

**Conclusion:** Following the implementation of care pathway, there has been no evidence of an accelerated decline in PF of our diabetic population. This indicates provision of systematic referral pathway for CFRD leads to integration of CF and DT yielding improved patient management and optimised outcome.

Table 1: Patients Demographics

	Total No. 164 (100 m)	Existing DM 29 (14 m)	New DM 21 (9 m)	IGT 34 (21 m)*	Normal 80 (56 m)
Median age	25	25	30	23	25
Age range	16–62	18–47	20–47	18–48	16–62
Mean BMI	22.5	20.8	22.4	22.3	23

\*Subsequent AR showed 10/34 IGT patients reverted to NGT

Table 2: Changes in patients' PF at subsequent AR

PF	CFRD	IGT	Normal
Improved	46%	35%	35%
Declined	44%	50%	40%
Unchanged	10%	15%	25%

**243 Overfilling in pancreatic enzyme preparations: still an unresolved issue**R. Foresti, L. Peloso, M. Anelli. *Eurand spa, Milano, Italy*

Given their inherent instability, all currently available Pancreatic Enzyme Preparations (PEPs) contain an “overfill”, in order to assure – at the end of their shelf life – at least 90% of the label lipase activity. The USP currently allows overfills up to 65%.

The actual lipase activity of a PEP capsule labeled at 10,000 IU, therefore, might theoretically vary – according to its “freshness” – from 9,000 to 16,500 units.

This variation in potency can potentially lead to efficacy issues, which may cause increased pill burden, unnecessary drug associations to compensate for loss of efficacy or “product switching”.

The FDA also noted the potential safety risk posed by overfilling and, in a recently published Guidance, it imposed a zero overfill for all PEPs to be marketed in the USA after April 2008.

The overfill issue was first studied by Whitehead who – after analysing several commercially available PEPs – reported overfills ranging from 14 to 39%.

We recently run a similar series of tests on 16 PEPs currently available in Europe and in the USA and found overfill ranging from 7% to 47%, with a median value of 32%. Since the PEPs analysed were on average 10–12 months old, the actual amount of overfill was probably underestimated.

Our findings confirm those reported earlier by Whitehead and suggest that none of the currently available PEPs complies with the zero overfill requirement of the FDA Guidance and, therefore, highlight a potential cause of suboptimal therapy with the currently available PEPs.

**References**

- Whitehead AM, Pharmaceutisch Weekblad Scientific Edition, 1998; 10: 197–201.  
FDA guidance for Industry: Exocrine pancreatic insufficiency drug products – submitting NDAs, April 2006.

**244 On which foods can pancreatic enzyme preparations (PEPs) be sprinkled?**D. Shepherd<sup>2</sup>, R. Foresti<sup>1</sup>, D. Sica<sup>1</sup>, M. Anelli<sup>1</sup>. <sup>1</sup>*Eurand Spa, Milano, Italy;* <sup>2</sup>*Eurand Inc, Vandalia, OH, USA*

In very young children with Exocrine Pancreatic Insufficiency it is a common practice to open the dosage units and to sprinkle their content on a small amount of food. The most commonly used food is “applesauce”, since its acidic pH preserves the coating of gastroprotected formulations which in turn prevents the degradation of the enzymes in the stomach. Since the coating of most enteric coated formulations starts dissolving at pH values above 5.5, it is safe to assume that all foods with pH ≤ 5 could be used as a “vehicle” for PEP particles.

We tested 26 different baby and infant foods commercially available in the US market and we found that 17 of them (66%) had a pH suitable for sprinkling. In order to obtain additional evidence on the suitability of this pH based approach, we tested also the “resistance” of three batches of EUR-1008 microtablets (a novel enteric coated PEP) on another series of commercially available foods. The foods tested included two simulations of “homemade recipes”, one with apple and one with banana, both with the addition of sugar and lemon juice. We considered as “suitable” those foods where EUR-1008 microtablets could remain for at least one hour, without any significant deterioration of the gastroresistant coating. Ten out of eleven (91%) foods, including both homemade recipes, proved to be suitable for the sprinkling/mixing of EUR-1008 microtablets.

Even though parents and caregivers should pay some attention to the foods they sprinkle the content of the PEP capsules on, in most cases where the “universally recommended applesauce” is not a feasible option, several other commercially available foods and even “homemade recipes” could be used as an alternative.

**245 A phase III trial of EUR-1008 in young cystic fibrosis (CF) patients with exocrine pancreatic insufficiency (EPI)**J. Wooldridge<sup>1</sup>, R. Amaro-Galvez<sup>2</sup>, K. Blake<sup>3</sup>, B. Chatfield<sup>4</sup>, S. McColey<sup>5</sup>, M.S. Woo<sup>6</sup>, C. Straforini<sup>7</sup>, M. Anelli<sup>7</sup>. <sup>1</sup>*Children's Hospital, Cincinnati, OH, USA;* <sup>2</sup>*Texas University, Tyler, TX, USA;* <sup>3</sup>*Nemours, Jacksonville, FL, USA;* <sup>4</sup>*Utah University, Salt Lake City, TX, USA;* <sup>5</sup>*Children's Hospital, Chicago, IL, USA;* <sup>6</sup>*Children's Hospital, Los Angeles, CA, USA;* <sup>7</sup>*Eurand SpA, Milan, Italy*

The study compared fat malabsorption and clinical symptoms in patients with CF before and after treatment with EUR-1008, a novel pancreatic enzyme formulation.

**Study design:** The multicenter, open label trial involved a 7d dose stabilization period and a 7d treatment period. Patients were switched from baseline enzyme treatment without wash-out.

**Inclusion criteria:**

1. age <7 y in acceptable nutritional status
2. confirmed CF and EPI,
3. no acute conditions
4. written informed consent

**Exclusion criteria:**

1. history or diagnosis of fibrosing colonopathy, hyperuricemia, hyperuricosuria or DIOS
2. recent use of immunosuppressive drugs, steroids or antibiotics
3. organ transplant or bowel surgery
4. hepatic insufficiency, hyperglycemia or CF-related diabetes

**Results:** 19 patients (12M, mean age 3.9, range 1–6) completed all phases of the study. The percentage of “responders” – patients without steatorrhea and signs and symptoms of malabsorption – was 52.6 at baseline, 68.4 (p=0.375 vs base) after stabilization and 57.9 (p=0.999 vs base) at the end of the study. Frequency and oily stools showed a significant decrease vs. baseline at end of study.

Physicians characterized patients as “improved” for 37% patients and “unchanged” in 63% at the end of the treatment phase. Parents characterized their children as 47% “improved” and 53% “unchanged”. No significant laboratory abnormalities or drug related adverse events occurred during the treatment phase.

**Conclusion:** EUR-1008 is an effective, safe, and well tolerated in the treatment of EPI in young CF patients.